Inconsistent analytic strategies reduce robustness in fear extinction via skin conductance response

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Abstract

Robustness of fear conditioning and extinction paradigms has become increasingly important for many researchers interested in improving the study of anxiety and trauma disorders. We recently illustrated the wide variability in data analysis techniques in this paradigm, which we argued may result in lack of robustness. In the current study, we resampled data from six of our own fear acquisition and extinction datasets, with skin conductance as the outcome. In the resampled and original datasets, we found that effect sizes that were calculated using discrepant statistical strategies, sourced from a non-exhaustive search of high-impact articles, were often poorly correlated. The main contributors to poor correlations were selection of trials from different stages of each experimental phase and use of averaged compared to trial-by-trial analysis. These findings reinforce the importance of focusing on robustness in psychophysiological measurement of fear acquisition and extinction in the laboratory and may guide prospective researchers in which decisions may most impact the robustness of their results.

Keywords: Skin conductance response, Statistical analysis, Fear extinction, Fear conditioning, Threat conditioning, Robustness

Introduction

Anxiety disorders are characterised by excessive and persistent aversive responses to neutral, safe, or ambiguous stimuli (Craske et al., 2009; Grupe & Nitschke, 2013). Similarly, deficient learning and retention of fear extinction has been proposed as a primary maintaining factor in anxiety and posttraumatic stress (PTSD) disorders (Graham, Callaghan, & Richardson, 2014; Grupe & Nitschke, 2013; Suarez-Jimenez et al., 2019; Zuj & Norrholm, 2019; Zuj, Palmer, Lommen, & Felmingham, 2016). Improved understanding of the underlying mechanisms of extinction could aid the development of clinical interventions for anxiety and traumatic disorders (Craske, Treanor, Conway, Zbozinek, & Vervliet, 2014; Lebois, Seligowski, Wolff, Hill, & Ressler, 2019).

Recent decades have seen increasingly sophisticated measurements of fear acquisition and extinction in the laboratory, with important implications for treatment of anxiety and PTSD (Milad & Quirk, 2012; Zuj & Norrholm, 2019). Fear acquisition paradigms model adaptive threat learning via contingent pairings of previously neutral conditioned stimuli (CS) and innately aversive unconditioned stimuli (US). Fear (or threat) extinction procedures feature repeated unreinforced presentation of the conditioned threat stimulus (CS+), leading to decreased threat responses and new safety learning that competes with previous threat memories (Bouton, 2004). Extinction learning and the subsequent retention of the extinction memory can be quantified by comparing the extinguished CS+ and the CS- during the extinction and retention phases respectively. Responses during the extinction phase can be used to index extinction learning itself, while differences at subsequent testing reflect retention or consolidation of extinction or retained fear memories (Lonsdorf et al., 2017; Milad & Quirk, 2012).

Phasic skin conductance responses (SCRs) constitute the most commonly used measure of conditioned threat responding (Bach et al., 2018; Lonsdorf et al., 2017; Pittig, Treanor,

LeBeau, & Craske, 2018). The amplitude of physiological responding to a threat signal (i.e., the CS+) can be compared to the safety signal (i.e., the CS-) to infer extinction. Physiological measures – especially SCRs – are notoriously noisy, with large degrees of individual variance and biological artefacts (Bach et al., 2018; Boucsein, 2012; Ojala & Bach, 2020). We had previously expressed concerns that, due to insufficient power in most studies, slight variations on core analytical strategies – such as choice of statistical analysis or removal of trials – might result in inconsistent findings in the same paradigm (Ney et al., 2018). The high-impact studies that we surveyed in this publication differed in the number and order of trials included in analysis, in which trials were averaged, and whether differential responding was used. Previously, high heterogeneity in experimental design and analysis of studies examining reinstatement effects following extinction was reported (Haaker, Golkar, Hermans, & Lonsdorf, 2014). More recently, Lonsdorf, Merz, and Fullana (2019) expressed concern that no consensus currently exists among fear extinction studies estimating the extinction retention index, which was originally developed as a way of inferring retention of extinction memory relative to responding during acquisition. Lonsdorf et al. identified 16 separate analysis strategies and showed that these strategies, despite claiming to be measuring a single underlying construct (i.e. extinction retention), were in fact partly poorly correlated and did not necessarily reflect extinction memory.

Research domains that are generally underpowered, have flexible outcomes and are evaluated using multiple analytical strategies are at high risk of poor replicability (Ioannidis, 2005; Simmons, Nelson, & Simonsohn, 2011). In the present study, we sought to examine the similarity of results produced by variations in statistical analyses of fear acquisition and extinction. Doing so was intended as an extension from Lonsdorf et al. (2019) where only the robustness of the extinction retention index was tested. Our aim was to test the robustness of the analytical strategies for analysing SCRs during acquisition and extinction learning from

high-impact studies. To do this, we performed a non-exhaustive literature search to gather several contrasting statistical strategies for similar fear conditioning paradigms. We then correlated the effect sizes of different methods obtained in across multiple of our own datasets, which we resampled to create a final sample of N = 40 datasets. We hypothesised that slight variations of analytical strategies would result in weak, non-significant correlational effect sizes, despite the methods purportedly measuring the same constructs.

Method

Method Selection

We searched online datasets (PubMed, PsycInfo, Web of Science) for keywords "fear acquisition", "fear conditioning", "fear extinction", "skin conductance" and "extinction". To ensure that we obtained a sufficiently influential yet not overwhelmingly large sample, articles that had 150 or more citations on Web of Science and were published post-2000 were included in the first-pass search. Due to datasets from our lab consisting of within-session CS+/- differential acquisition paradigms with SCRs as the primary outcome measure, there were several restrictions on the studies that were included. Firstly, we did not include studies that had used contextual or additional CS+ manipulations during fear acquisition or extinction learning. Second, we only included analyses from day 1 of multi-day paradigms, so long as they included both fear acquisition and extinction learning phases in a single session. Finally, only studies using SCRs as a primary outcome measure were included, since SCRs are the predominant acquisition measure and there has been significant heterogeneity in its scoring and reporting. Strategies were separated into three categories. Some studies had focused on the difference between SCRs from the acquisition to extinction phase (ACQ-EXT), whereas others were either interested in the change of SCRs over the extinction phase (EXT_{early}-EXT_{late}) or in estimating a gross measure of fear extinction learning during that phase (EXT). We were aware

of several other articles with fewer than 150 citations that had used unique analysis strategies; these were added to increase the pool of strategies for the ACQ-EXT and EXT_{early}-EXT_{late} methods (see Table 1).

Datasets

We used data from six of our own datasets for this analysis (details below). To increase the sample size, data were resampled with replacement from the six datasets to create an additional 34 datasets of $N = 60$ each. Resampling was performed using the Resampling Stats Add-in for Excel v4.0 (Simon, Bruce, & Troiana, 2013). Resampling with replacement was preferred to ensure higher variability of the resampled datasets to the original datasets. To ensure that resampled datasets would mimic interphase correlations of SCRs, we resampled by row; that is, each resample consisted of the entire phase of one participant's CS+ or CS- response (but not both). This ensured that the data would mimic real responding as closely as possible without resampling any participant's entire differential response.

All datasets used either red and blue (datasets 1, 2 and 3) or green and orange (datasets 4, 5 and 6) circles as CS, presented on a computer screen. In all studies, CS+ and CS- were randomised between participants. CS duration was 12s with intertrial intervals of 12-21s (M = 16s). Each study consisted of three phases: habituation, acquisition and extinction learning. Habituation lasted for 4 trials (ie. 4 separate presentations of CS+ and 4 of CS-) and the extinction phase consisted of 10 trials. Datasets 1-3 featured 5 acquisition trials, while datasets 4-6 had 7. For the latter datasets, only the first 5 trials were analysed, so to be consistent with datasets 1-3 during analysis and resampling. Although datasets 3-6 were 2-day paradigms, only the first day was used so as to be consistent with datasets 1 and 2. Datasets 1-3 had a 100%

CS-US reinforcement schedule during acquisition, whereas the other datasets had a 62.5% schedule.

Each of the original datasets had a different group manipulation. For datasets 1-3 (N = 120, N = 56 and N = 79, respectively) participants consisted of PTSD-diagnosed cases, trauma-exposed cases and non-trauma exposed cases (each dataset had a different manipulation outside of this, see publications or Supplementary Material for additional details; Hsu, et al. in prep; Ney, et al. in prep; Zuj, et al. 2016). In dataset 4, the group manipulation was sham or anodal transcranial direct current stimulation (tDCS) to the dorsal lateral prefrontal cortex prior to or following the extinction learning phase (N = 80, Ney et al., in prep; Vicario et al. , 2019). In dataset 5 the group manipulation was naturally cycling women in the early follicular phase of the menstrual cycle compared to women in the midluteal phase and men (N = 48, unpublished data). In dataset 6 the group manipulation was a laboratory stress induction (the MAST; Smeets, et al. 2012) either immediately following acquisition or immediately prior to extinction (N = 45, Ney, et al. 2018). In all datasets, participants had no neurological or cardiovascular illnesses, no history of head injury or loss of consciousness, no drug use, no heavy alcohol use and no psychiatric illnesses, other than PTSD in datasets 1-3.

Given the goals and framework of this study, it is unlikely that variability in data collection methods (e.g. reinforcement ratio) or experimental manipulations would affect results. This is because the predictor variable in our study is the analysis method itself. As such, our primary concern was to produce data that reflected data obtained during real experiments wherein any effects observed were the differences between analysis strategies due to all datasets being tested by all strategies.

Apparatus and Data Reduction

In all studies a stimulus isolator (ADInstruments) was attached to the right hand and participants were encouraged to choose a US level that was "highly uncomfortable but not painful". The 500 ms electric shock was delivered at CS+ offset during the fear acquisition phase. Galvanic skin conductance was recorded in micro-Siemens (μS) using a 22 mVrms, 75 Hz constant-voltage coupler (ADInstruments). Electrodes were strapped to the second phalanges of the first and third fingers of the left hand. SCRs to the CS+ and CS- were preprocessed using the PsPM toolbox v4.2.1 in MATLAB (version 9.7) (Bach & Friston, 2013; Bach, Friston, & Dolan, 2013). Using custom coding, we used a peak scoring interval of 0.9-5s following stimulus onset, given that SCRs peak within a relatively narrow window following CS onset, called the first interval response. However, this choice does not necessarily reflect a standardised latency interval as currently this does not exist (see Jentsch et al. 2020; Pineles et al. 2009). In order to remove noise in the data, a bidirectional Butterworth filter (1.5Hz low pass; 0.5Hz high pass) was applied to the raw SCR trace.

Statistical Analysis

In all analysis strategies, we aimed to test the stimulus × trial × group effects. For some methods this meant that the analysis was actually a trial × group, or even phase × group interaction, since some methods used differential responses (calculated by subtracting a CS- response from the adjacent CS+ response) or averaged responses (either differential or CS+/CS- over successive trials, see Table 1). From each analysis we obtained a partial eta squared effect size for this interaction. Kendall non-parametric ranked order correlation coefficients (τb) were run on the effect size from each dataset for each of the three categories of analysis. Bayes factors and 95% credible intervals were calculated based on each correlation. This approach was favoured over p-values due to significant values being easily achieved in large sample sizes of simulated data. Further, credible intervals allow more accurate

interpretation of the possible range of the effect size relative to confidence intervals (Morey, Hoekstra, Rouder, Lee, & Wagenmakers, 2016). To ensure that our resampled datasets did not bias the data, correlations were run and compared with both the original sample (N = 6, see Supplementary Material) and the resampled sample (N = 40). All data analyses were conducted in Jamovi 1.1.9. Bayesian analyses were conducted using the jsq module.

Results

Over 5,000 unique articles were identified in the search. Fifteen articles were selected as they met the following criteria: over 150 citations, fear conditioning and extinction phases, human only, and using skin conductance. Additional articles that had been cited less than 150 times were also included to increase the number of different methods examined (strategies 3 and 4 in Acquisition-Extinction, Strategy 2 in Extinction, and Strategy 5 in Extintion-Extinction, Table 1). Therefore, this is a small, yet exemplary sample of the methods used in the fear conditioning literature.

As in Lonsdorf, Merz, et al. (2019), we observed a high heterogeneity of analytical strategies (Table 1). In Table 1, each strategy is assigned to a category based on how the phases were analyses (i.e. comparing acquisition-extinction, extinction as a whole or comparing early extinction-late extinction). The study that used each strategy is specified in the rightmost column. The differences between these strategies included how many trials were included in the study (column 3, Table 1), how many trials from these were included in the analysis (column 4, Table 1), whether these trials were averaged or assessed on a trial-by-trial basis (column 5, Table 1), whether the CS+/CS- trials were included as a single differential response (column 6, Table 1), and what final statistical method was used (column 7, Table 1). Different combinations of these variables lead to a potentially wide array of statistical strategies. We noted heterogeneity in the number of trials retained during the analysis, regardless of how many

trials were originally present in the study. There was also inconsistency in whether selected trials were averaged or compared on a trial-by-trial basis, as well as whether differential responses were calculated. Resulting statistical analyses were more homogenous, with mixed ANOVAs being used across all high-impact studies.

Acquisition-Extinction

Strategies for the first set of analyses, where change in responding from acquisition to extinction learning is assessed, were relatively similar (Table 1). All four strategies used average differential responses, and two of the four drew trials from the whole acquisition phase. One of the other strategies used the trials from the second half of acquisition, whereas the other strategy used the single highest differential response from acquisition. Two of the four strategies used the final two trials of extinction learning, one used the last three out of seven trials and the final used the first half of extinction trials.

Insert Table 1 about here

Static Extinction

For the second set of analyses, we compared strategies from studies assessing extinction learning as a static construct (EXT) that could be compared to responses in other trials or studies. This group of strategies did not measure change in responding across or within extinction learning phases and instead estimate the gross responding during extinction learning. Four out of seven compared CS+ and CS- responses, whereas the other three used differential responding. Three used trial-by-trial analyses; though, of these, one used only the first two trials, one used all trials, and the final one used a "running average" response, where trials one and two were averaged as a single response, trials two and three were averaged, and so on.

Three strategies used averaged responses, with one using the final quarter of extinction trials, one using the last half and one using the last two trials. Strategy 4 used only one trial; this was the last trial.

Early Extinction vs. Late Extinction

For the final set of analyses, we compared the strategies from studies that assessed change in extinction learning across the extinction phase. Trial-by-trial analysis was not sufficient to fit to this category, since ANOVA that fits trial as a parameter does not account for the order of the trials. Three of the five strategies compared the average of the first half of trials to the average of the second half of trials, though one of these strategies used differential responses, one only used CS+ responses and the other retained the CS+ and CS- as separate responses. One of the strategies assessed, the average CS+ responses in the first quarter of extinction to the final quarter of extinction, and the final strategy assessed CS+ and CS- separate responses using linear trends across all trials.

Correlations

Tables 2-4 show Kendall rank correlation coefficient values (τb) for the three different sets of analyses. For strategies comparing acquisition and extinction phases, correlations were high between Strategies 1-3 (Table 2). Strategy 4 did not produce reliable results compared to the other methods. For strategies producing a static estimate of extinction learning (Table 3), correlations were more inconsistent, ranging from τb = -.062 to τb = .602. Only seven comparisons between the all combinations of the seven strategies produced correlations that were supported by Bayes factors and 95% credible intervals, though some of these were very highly supported. The final set of strategies performed similarly to acquisition, with six out of ten comparisons of the five strategies producing supported correlations. These correlations

ranged from $_Tb$ = .060 to $_Tb$ = .982, with Strategy 1 and Strategy 2 being almost exactly similar, but Strategy 5 being dissimilar to all the other strategies.

Insert Tables 2-4 about here

Discussion

Previous studies have reported high heterogeneity in the indexation and analysis of extinction retention and reinstatement between fear conditioning and extinction paradigms (Haaker et al., 2014; Lonsdorf, Merz, et al., 2019; Ney et al., 2018). In this study we compared analytical strategies that assessed fear extinction learning in human SCR paradigms in several datasets that were resampled from our laboratory's data. A high degree of heterogeneity was found between the strategies, with choices such as which trials to use during analysis, whether to use differential responses and whether to average trials or use trial-by-trial analysis all differing significantly between studies. Using a bootstrapped dataset based on six of our own datasets, we found that correlations between the strategies used in these studies were usually poor, even though they were intended to estimate similar constructs. We found this was true particularly for studies estimating SCRs both statically and across extinction learning, though strategies that assessed change between acquisition to extinction phases were relatively reliable. These findings have implications for the reliability of psychophysiological studies of fear acquisition and extinction learning.

When considering changes in SCRs from acquisition to extinction learning, strategies that compared average or maximal differential values during acquisition to average differential values at the end of extinction learning were highly correlated, regardless of the trials that were included. Strategy 4 of this category, which compared the average differential trials from late acquisition to early extinction was poorly correlated with the other strategies.

We can surmise from this that it is likely that studies that compare different stages of each phase from acquisition to extinction may not be comparable. However, it should be noted that we had less acquisition trials compared to many other studies and this finding may not generalise to paradigms with more trials.

During extinction learning Strategies 1 and 3 were highly correlated, with the only difference being the inclusion of a quarter of the extinction trials. However, when strategies selected from different sections of extinction, they were poorly correlated. This was also reflected in the early-late extinction category, with Strategies 3 and 4 being significantly correlated. This again suggests that analyses during extinction are relatively insensitive to minor variations in trial selection, so long as sufficiently large numbers of trials are selected from the same quadrants of the phase. Using linear trends rather than omnibus ANOVA resulted in vastly different effect sizes. Interestingly, the evidence here also shows that use of differential compared to separate CS+/CS- responding may not impact robustness, with high correlations observed in both Categories 2 and 3 between studies that used identical parameters apart from this. It can therefore be concluded, based on these data and with relatively homogenous trial numbers between studies, that selection of trials from contrasting segments of paradigm phases and discrepant use of trial-by-trial compared to averaged data present the major risks to robustness.

We have previously made several recommendations that may improve robustness in the fear conditioning paradigm (Ney et al., 2018). Here, we maintain that graphing trial-by-trial data and increasing sample size are ways to improve transparency and robustness that any laboratory should be readily able to implement with minimal effort and resources. Similarly, the transparency and robustness of research might be improved by any laboratory by adopting a multiverse approach, where multiple analyses are conducted on the same data to elicit the reliability of reported findings from one approach (Silberzahn et al., 2018;

Steegen, Tuerlinckx, Gelman, & Vanpaemel, 2016). These approaches rely on increased transparency in data reporting and analysis, and we maintain that decisions during data reduction and analysis should be reported and justified (Lonsdorf, Klingelhöfer-Jens, et al., 2019; Ney et al., 2018). It is also possible that reproducibility may be improved by computational optimization of paradigm design, which may aid in determining how to vary experimental parameters to answer specific research questions (Melinscak & Bach, 2020).

Based on the current data, however, we make several specific recommendations that may improve robustness. Firstly, future research should recognise that learning between early and late stages of an extinction phase are unlikely to be comparable, since differential selection of these time periods presented the greatest impairment to robustness in the present study. Future studies should aim to specify and further characterise the differences in learning that occur in early compared to late extinction trials so that it can be better understood at which stage of learning clinical participants show the most impairment, or treatments show the most efficacy. Similarly, the cause for inadequate robustness between trial-by-trial and averaged data should be systematically investigated. It is possible that the failure of these methods to replicate is due to lack of power, in which case methods that seek to improve power via experimental design and SCR scoring are highly desirable (Bach & Melinscak, 2020; Melinscak & Bach, 2020). Specifically, improving SCR scoring can provide better estimates of responses relevant to extinction paradigms by reducing measurement error (Bach & Melinscak, 2020), and optimisation of experimental designs based on statistical requirements can make analyses more amenable to experimental data (Melinscak & Bach, 2020). Both of these methods can improve experimental power without additional participant recruitment.

While reducing measurement error during pre-processing of data can improve power, a greater understanding of the mechanisms that shape fear extinction learning could also be

achieved through implementation of computational learning models of processed data. Model-based analysis has previously been used to characterize dissociable striatal and amygdala contributions to fear conditioning (Delgado et al., 2008; Li et al. , 2011; Schiller et al., 2008), accounting for genetic, affective, and cognitive individual differences in fear learning (Baetu et al., 2018; Laing, Burns, & Baetu, 2019), and identifying exaggerated neural prediction errors in PTSD symptomology (Homan et al., 2019). Tzovara et al. (2018) recently found that both SCRs and pupil responses during conditioning were best explained by a Bayesian learning model, though reflected slightly different aspects of learning during the task . However, these models, as well as Bayesian learning models that parameterize uncertainty (Gershman & Hartley 2015; Tzovara, Korn, & Bach 2018), have thus far only been applied to human fear conditioning in a limited way. Computational modelling is advantageous because it formalises statistical decision-making to allow statistical choices between studies to be explicitly compared. Comparison and selection of best statistical methods requires complete transparency of justifications for different choices and aims to formally determine the most representative model for a particular experimental design. For this reason, modelling adheres very closely to the goals of open science and represents the best practices in statistical analysis (Adams, Huys, & Roiser, 2016). Therefore, by mathematically expressing what we expect to occur in SCR data during extinction learning, we can assess the validity our existing ideas of how extinction learning impacts physiological responding. With this level of formalism, methodological decisions are required to be justified and compared to competing frameworks.

One limitation of the current study is that the level of heterogeneity found here may not generalise to other data processing methods, such as model-fitting techniques such as PsPM where study power is maximised (Bach & Melinscak, 2020). Further, significant work will need to be conducted before standardisation of statistical analyses of this paradigm may

be achieved; here we have only indicated that systemic issues exist in the current approach. Modelling approaches will also need to be tailored to suit different paradigm designs to accommodate parameters such as trial length (Bach & Melinscak, 2020). Our paradigm also featured a relatively small number of trials, particularly during acquisition. Therefore, our conclusions of high correlations between certain methods may not generalise to studies with more trials and cannot be generalised to differing experimental designs such as delayed extinction. Finally, due to the high heterogeneity of strategies anticipated in a literature search, our included studies were compiled toprovide an exemplary, yet non-exhaustive, representation of strategies used in the field. Although many of the studies here were chosen on the basis of number of citations rather than statistical methods, larger syntheses of the literature may reveal less heterogeneity and higher robustness than we observed here. Similarly, differences in the original data included here as derived from different studies may have caused higher variance in the data and potentially impacted our results.

In summary, we provide evidence of limited robustness between SCR fear extinction studies due to variation in analytical strategy. The highest impact on robustness was evidenced by differential trial selection from contrasting halves of extinction learning, as well as the use of trial-by-trial compared to averaged analyses. We conclude that, in order to enhance reliability, future studies should investigate the differences in extinction learning that occurs between early and late extinction phases. We have also made several suggestions that could improve the robustness of the current paradigm, including improving sample sizes, visualising SCR data points, improving transparency of data reporting, and computational modelling of extinction learning.

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Tables

Table 1. Description of different strategies for measuring extinction learning using skin conductance responses

Analytic strategy	Strategy #	# of Trials	Trials Included	Trial Analysis	Stimuli Analysis	Analysis	Study
ACQ - EXT	Strategy 1	8 (ACQ), 16 (EXT)	All (ACQ), last 2 (EXT)	Average	Diff	Phase×group	Graham & Milad, 2013
	Strategy 2	5 (ACQ), 10 (EXT)	Maximum Response (ACQ), Last 2 (EXT)	Average	Diff	Phase×group	Milad, et al. 2010
	Strategy 3	8 (ACQ), 7 (EXT)	All (ACQ), last 3 (EXT)	Average	Diff	Phase×group	White & Graham, 2016[#]
	Strategy 4	20 (ACQ), 20 (EXT)	Last half (ACQ), First half (EXT)	Average, using paired t-test contrasts^	Diff	Phase×group	Grady, et al. 2016[#]
EXT	Strategy 1	16	Last three-quarters	Average	CS+, CS-	Group×stim	Milad, et al. 2009;
	Strategy 2	5	All	Trial-by-trial	CS+, CS-	Trial×Group×Stim	Zuj, et al. 2016[#]
	Strategy 3	16	Last half	Average	CS+, CS-	Group×stim	Garfinkel, et al. 2014

	Strategy 4	10	Last trial	One trial	Diff	Group	Schiller, et al. 2010
	Strategy 5	10	Last 2	Average	CS+, CS-	Group×stim	Milad, et al. 2008
	Strategy 6	5	All	Running average[#]	Diff	Trial×Group	Milad, et al. 2006
	Strategy 7	8	First 2	Trial-by-trial	Diff	Trial×Group	Pace-schott, et al. 2013[#]
EXT_{early}-EXT_{late}	Strategy 1	6	First half, second half	Average	CS+, CS-	Phase×Group×Stim	Blechert, et al. 2007
	Strategy 2	14	First half, second half	Average	Diff	Phase×Group	Michael, et al. 2007; Phelps, et al. 2004
	Strategy 3	16	First quarter, last quarter	Average	CS+	Phase×Group	Milad, et al. 2013
	Strategy 4	32, 16	First half, second half	Average	CS+	Phase×Group	Soliman et al., 2010; Zeidan et al., 2011
	Strategy 5	10	All	Linear contrast	CS+, CS-	Trial×Group×Stim	Lovibond et al. (2009) [#];

				Ney, et al. (in prep) [#]

ACQ = Acquisition, EXT = Extinction, Diff = Differential, CS+ = Conditioned stimulus to the aversive unconditioned stimulus, CS- = Conditioned stimulus as a safety signal, Stim = stimulus type (CS+ v. CS-). ^This study was the only study to use a test other than ANOVA. [#]Running average response was calculated with trials one and two averaged as a single response, trials two and three averaged, and so on. [#]Study was not identified as part of the original search criteria but was added post-hoc due to methodological variance.

Table 2. *Acquisition – Extinction.* Strategy comparisons using Kendall rank correlation coefficient between datasets with changes from acquisition to extinction learning phases estimated

		Strategy 2	**Strategy 3**	**Strategy 4**
Strategy 1	$_{T}b$	.609	.794	.125
	BF	571814***	1.55E+10***	.4
	95%CI	**[.76,.36]**	**[.90,.52]**	[.32,-.09]
Strategy 2	$_{T}b$		.558	.044
	BF		52991***	.2
	95%CI		**[.71,.31]**	[.24,-.16]
Strategy 3	$_{T}b$			.152
	BF			.5
	95%CI			[.35,-.06]

N = 40 datasets with correlations comparing strategies conducted in all datasets. $_{T}b$ = Spearman's *R* coefficient. 95%CIs are 95% credible intervals. ***BF>30, **BF>20, *BF>10.

Table 3. *Static Extinction.* Strategy comparisons using Kendall rank correlation coefficient between datasets with a static extinction learning efficacy estimated

		Strategy 2	**Strategy 3**	**Strategy 4**	**Strategy 5**	**Strategy 6**	**Strategy 7**
Strategy 1	$_{T}b$	.047	.488	.252	.332	.075	.020
	BF	.2	2799***	3	17*	.3	.2
	95%CI	[.25,-.16]	**[.65,.25]**	**[.44,.03]**	**[.51,.10]**	[.27,-.14]	[.22,-.19]
Strategy 2	$_{T}b$		-.008	-.014	-.010	.602	.483
	BF		.2	.2	.2	408227***	2370***
	95%CI		[.20,-.21]	[.19,-.22]	[.19,-.21]	**[.75,.35]**	**[.65,.24]**
Strategy 3	$_{T}b$			.102	.425	.012	.001
	BF			.3	283***	.2	.2
	95%CI			[.30,-.11]	**[.60,.19]**	[.21,-.19]	[.20,-.20]
Strategy 4	$_{T}b$				.371	-.031	-.062
	BF				51***	.2	.2
	95%CI				**[.55,.14]**	[.17,-.23]	[.14,-.26]
Strategy 5	$_{T}b$					-.052	.006
	BF					.2	.2
	95%CI					[.15,-.25]	[.20,-.21]

Strategy 6	$_{T}b$	.152
	BF	.5
	95%CI	[.34,-.06]

N = 40 datasets with correlations comparing strategies conducted in all datasets. $_{T}b$ = Spearman's *R* coefficient. BF is the Bayes Factor. 95%CIs are 95% credible intervals. ***BF>30, **BF>20, *BF>10. CIs that do not cross zero are bold.

Table 4. *Early – Late Extinction.* Strategy comparisons using Kendall rank correlation coefficient between datasets with changes during extinction learning estimated

		Strategy 2	**Strategy 3**	**Strategy 4**	**Strategy 5**
Strategy 1	$_{T}b$	.982	.340	.295	.060
	BF	4.89E+15***	21**	7	.2
	95%CI	**[.97,.67]**	**[.52,.11]**	**[.48,.07]**	[.26,-.15]
Strategy 2	$_{T}b$		.358	.308	.068
	BF		35***	9	.2
	95%CI		**[.53,.13]**	**[.49,.08]**	[.27,-.14]
Strategy 3	$_{T}b$			.630	.080
	BF			1.53E+6***	.3
	95%CI			**[.77,.38]**	[.28,-.13]
Strategy 4	$_{T}b$				.083
	BF				.3
	95%CI				[.28,-.13]

N = 40 datasets with correlations comparing strategies conducted in all datasets. $_{T}b$ = Spearman's *R* coefficient. 95%CIs are 95% credible intervals. ***BF>30, **BF>20, *BF>10. CIs that do not cross zero are bold.